REMARKS

Claims 1-6, 20-24, 32 and 38-49 are pending and all pending claims were rejected in the Office Action. Claims 1-6 and 38-42 have been canceled without prejudice to future presentation. Claims 20, 43, 47 and 49 have been amended and new claims 50-57 have been added. It is believed that these amendments do not constitute new matter and their entry is requested.

35 U.S.C. 112 first paragraph rejection

Claims 1-6 and 38-42 stand rejected under 35 U.S.C., 112, first paragraph, for lack of enablement. The Examiner has acknowledged that the specification is enabling for claims directed to a method for deleting nucleic acids in a specific tissue of a mouse but has asserted that the claims are not enabled for this method in other organisms. Claims 1-6 and 38-42 have been canceled. Presently pending claims 43-57 encompass methods for the deletion of a nucleic acid from a mouse or mouse cell or tissue. For at least these reasons, it is believed that the claims as amended are enabled and withdrawal of this rejection is requested.

35 U.S.C. 102(e) rejection

Claims 1-6, 20-24, 32, 38-41 and 43-45 were rejected under 35 U.S.C. 102(e) as anticipated by U.S. Patent No. 6,537,805, which issued to Melchner et al. (Melchner) March 25, 2003. The Examiner is of the opinion that Melchner discloses a nucleic acid with a recombinase gene and a suicide gene, each operably linked to a promoter, and flanking sequences containing recombinase target sequences. The recombinase gene can be Cre or Flp and the flanking recombinase sequences can be Lox or Frt. The effective filing date for purposes of 35 U.S.C. 102(e) for Melchner is June 12, 2000. The present application claims priority to a provisional application filed June 29, 1999, a date which has been acknowledged by the Examiner in Paper Number 10.

Based on the foregoing, it is respectfully submitted that Melchner is not 102(e) prior art to the present application and withdrawal of this rejection is requested.

35 U.S.C. 112, second paragraph rejection

The Examiner has rejected claims 20-24 and 43-49 under 35 U.S.C. 112, second paragraph, for being indefinite. Claim 20 and the claims which depend from this claim were rejected for being indefinite for reciting a "foreign" DNA. The Examiner is of the opinion that these claims are unclear because it is unclear if the foreign DNA is "[f]oreign to the construct, or to the recipient animal it would be used in, or foreign to both?" (Office Action of 5/8/03 at page 9). The Examiner also asserts that it would appear that "'foreign' is dependent upon the context in which the molecule would be used...[and also that]...the term foreign DNA encompasses any sequence, expressed or not, even a few base pairs." (Id. at page 10).

Claim 20 has been amended to recite a nucleic acid molecule for removing a foreign DNA that has been inserted into a host cell genome. Thus, it is clear that the term "foreign" is made with reference to the host cell. The present specification notes at page 4, lines 17-21, that the "foreign" DNA may be heterologous DNA, such as a marker sequence, or it may be a wild-type allele, such as for use in gene therapy. The foreign DNA molecule may further contain a gene which is desired to be incorporated into the transgenic organism or into tissue in the organism. Furthermore, the foreign DNA can encompass "even a few base pairs" if it is these base pairs comprise the sequence which is to be removed from the genome after insertion, such as, for example in the case of a marker sequence.

Based on the amendment to claim 20, it is believed that claims 20-24 particularly and distinctly point out the subject matter of the invention.

Claim 43 was rejected for reciting a recombinase gene expressed in a tissue, while the claim recites a method for deleting a molecule that has been introduced into a cell.

Claim 43 has been amended to recite a method wherein the recombinase gene is expressed in said cell.

Claim 47 was rejected as lacking antecedent basis for the step of introducing a DNA molecule into an organism, since the claim depends from a claim that recites introducing the DNA molecule specifically into a mouse. In addition, the Examiner has objected to the language of claim 47 for omitting essential steps of generating a transgenic organism. Claim 47 has been amended to recite a method as in claim 43 which is performed *in vivo* in a mouse during gametogenesis.

Claim 49 was rejected as unclear because the Examiner is of the opinion that in order for a mouse to be considered transgenic (as opposed to chimeric), the transgene must be stably integrated into the mouse genome. Claim 49 has been amended to recite a transgenic mouse wherein the DNA molecule has been stably integrated into the mouse genome.

Based on the amendments to the claims and the foregoing comments, it is believed that the claims particularly and distinctly point out the subject matter of the invention and withdrawal of this grounds of rejection is requested.

In view of the above remarks and amendments, Applicants believe that the Examiner's rejections set forth in the previous and outstanding Office Actions have been overcome and that the present application is in condition for allowance. The Examiner is

invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

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